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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,528	01/29/2004	Karl Salzwedel	1900.0430002/LBB/SJE	2237

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,528	SALZWEDEL ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,10,12,13 and 82-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,10 and 82-84* is/are rejected.

7)☒ Claim(s) *12 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 July 2007 has been entered.

Applicants' request for interview has been noted. However, Applicants did not indicate what issues they desire to discuss at the interview. An interview should be had only when the nature of the case is such that the interview could serve to develop and clarify specific issues and lead to a mutual understanding between the examiner and the applicant, and thereby advance the prosecution of the application. MPEP §713. Since there are outstanding rejections in this case and Applicants have already responded to the rejections, an interview at this time does not advance the prosecution of the application. Therefore, an interview is not granted.

Claims 8, 11 and 14-81 have been cancelled. Claims 1-7, 9, 10, 12, 13 and 82-84 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 12 and 13 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in view of Applicants' argument that claims 12-13 recite particular compounds, which do not encompass the broad range of unrelated compounds listed in the previous Office Action.

However, the rejection of claims 1-7, 9, 10 and 82-84 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is **maintained**. Applicants' arguments have been fully considered and are not persuasive.

The instant claims are drawn to a method of treating HIV-1 infection in a patient, comprising orally administering to a patient in need thereof a compound that inhibits HIV-1 maturation, wherein upon contacting said compound with an HIV-1 infected cell and lysing said HIV-1 infected cell to form a lysate, said lysate exhibits a p25 (CA-SP1) band in a Western Blot assay and wherein the HIV-1 is resistant to HIV therapies having a mechanism other than maturation inhibition.

Applicants argue that Examiner's statement of the claim limitations encompassing siRNA, aptamers, ribozymes, antibodies, peptidomimetics, or homologs of Gag-binding proteins is not reasonable interpretation of the claims because the specification does not disclose these compounds. Therefore, Applicants actually are admitting that the specification does not support the other subgenera of siRNA, aptamers, ribozymes, antibodies, peptidomimetics, or homologs of Gag-binding proteins. Applicants' assertion of the meaning of the claim limitation "compound" is not consistent with the dictionary definition of the word "compound," which is a pure

substance composed of two or more elements whose composition is constant. The interpretation of the claims are not limited to the examples given in the specification only, especially since the specification does not define the term "compound" to mean strictly the small molecule chemicals. The pending claims must be "given their broadest reasonable interpretation consistent with the specification," MPEP §2111[R-5].

Applicants further argue that none of the siRNA, aptamers ,ribozymes, antibodies, peptidomimetics, and homologs of Gag-binding proteins can be administered orally. Applicants' assertion lacks evidentiary basis and does not address the issue of the lack of structural support for the genus of "a compound that inhibits HIV-1 maturation." In summary, Applicants' arguments do not facilitate the specification to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The rejection of claims 12 and 13 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement is **withdrawn** in view of Applicants' Exhibits C-F showing the clinical trials data of bevirimat (PA-457), which is 3-O-(3',3'-dimethylsuccinyl) betulinic acid, and an analog, PA-040.

The rejection of claims 1-7, 9, 10 and 82-84 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement is **maintained** because the specification, while being enabling for treating HIV-1 infection in a patient with betulinic acid derivatives, does not reasonably provide enablement for treating HIV-

1 infection with any other compound. Applicants' arguments have been fully considered but are not persuasive.

The instant claims are drawn to a method of treating HIV-1 infection in a patient, comprising orally administering to a patient in need thereof a compound that inhibits HIV-1 maturation, wherein upon contacting said compound with an HIV-1 infected cell and lysing said HIV-1 infected cell to form a lysate, said lysate exhibits a p25 (CA-SP1) band in a Western Blot assay and wherein the HIV-1 is resistant to HIV therapies having a mechanism other than maturation inhibition.

Applicants argued that the Examiner has not provided relevant and specific evidence that is published around the filing date. Applicants dismissed the prior art cited in the rejection by arguing that the case law *Ex Parte Balzarini* in 1987, the Martinez-Picado (1998) and Gait and Karn (1995) publications are not relevant to the period of time of the filing of the instant application. Applicants further alleged that the Lee (2003) reference cited by the Examiner refers to a nucleoside analog and is irrelevant to the claimed compounds. Applicants concluded that the Examiner has not provided sound scientific reasoning to suggest that the practice of the currently claimed methods would not have enabled a person of ordinary skill to treat HIV-1 infection in a patient. Applicants further asserted that the references supplied by the Examiner in the rejection do not suggest that the claimed methods would not be able to treat HIV-1 infection in patients. Applicants further argued that the specification provides *in vitro* data on DSB's anti-HIV activity and its toxicity and that references cited in the

specification disclose additional in vitro data on he anti-HIV activity of other molecules that fall within the scope of the recited compound.

In response to applicant's argument based upon the age of the references and the case law, *Ex Parte Balzarini*, contentions that the reference patents are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

Even though the Lee (2003) reference teaches nucleoside analogs, the reference also emphasizes the importance of the study of serum half-life, bioavailability, clearance of the drugs themselves, cellular uptake, transport, and metabolic activation of any drug compounds. These parameters are widely used for drug screening, which is well known to one skilled in the art.

While arguing that the Examiner's references do not literally deny the enablement of the claimed invention, Applicants failed to address the lack of structural guidance of the genus of all compounds that inhibit HIV-1 maturation. While disregarding Examiner's references teaching a high level of unpredictability in the art of HIV inhibitors, Applicants failed to provide any objective evidence showing the serum half-life, bioavailability, clearance of the drugs themselves, cellular uptake, transport, and metabolic activation of the claimed compounds, which are important properties that are required to address the unpredictability taught in the state of the art.

The *in vitro* data of DSB in PBMC does not enable the full scope of the claimed method as DSB does not represent the entire genus of HIV-1 maturation inhbitors. The

art teaches a lack of correlation between in vitro cell culture data and in vivo due to the vast difference between cell culture and animal or human bodies. In addition, the *in vitro* data cannot predict the drug delivery problems with respect to plasma concentration and serum sequestration as taught in the Karn (1995) and Lee (2003) reference. Exhibit B provided by Applicants are about side effects from reverse transcriptase inhibitors, which are not predictive of the pharmaceutical effects of the compounds used in the claimed invention.

Exhibits C-F provided by Applicants show the clinical studies of the claimed method of treatment with a specific maturation inhibitor, 3-O-(3',3'-dimethylsuccinyl) betulinic acid (PA-457, Bevirimat), and its analogs, which do not support the full scope of the claimed invention. The instant claims do not recite any structural limitations of the compound that inhibits HIV-1 maturation, thus the instant claims encompass treating HIV-1 infection in patients with, other than betulinic acid derivatives, many compounds that are not enabled by the specification and exhibits. The specification and the submitted exhibits do not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim Objections

Claims 12 and 13 are objected to for depending from a rejected base claim. Applicants are advised to rewrite claims 12 and 13 in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
21 September 2007

Louise Humphrey, Ph.D.
Assistant Examiner